REMARKS

Applicants have canceled claim 1 without prejudice and have amended claims 3 and 4 in order to more particularly point out the presently claimed invention. Applicants have introduced new claim 21 to more particularly point out the claimed invention. Support for claim 21 may be found throughout the application, for example on page 8, lines 1-34 and in Figure 1. In addition, applicants point out that they have disclosed administration of the protein encoded by the nucleic acid claimed and therefore support the isolation thereof. Applicants maintain that these amendments raise no issue of new matter. Thus, claims 3, 4 and 21 are pending.

Rejection Under 35 U.S.C. §112, second paragraph

The examiner rejected claims 1, 3 and 4 under 35 U.S.C. §112, first paragraph. The examiner stated that the referral to sequence of Figure 1 somewhat clarifies the basis of rejection but is improper. The examiner pointed out that 37 C.F.R. §1.821 states that where the description or claims of a patent application discuss a sequence that is set forth, reference must be made to the sequence by use of the sequence identifier, preceded by SEQ ID NO: in the text of the description or claims. The examiner stated that upon further consideration, reference to human or mouse CRAF1 is vague and indefinite because the reference is to an arbitrary name.

With regard to "CD40-mediated cell activation," the examiner stated that Potocnik et al. do not teach regarding the metes and bounds of "CD40-mediated cell activation." Potocnik et al. teach that CD40 expression is upregulated on T cells from RA patients. The examiner stated that whether those T cells are activated and if such activation is mediated by CD40 is not addressed, nor are any other cells addressed. Similarly, the

examiner stated that the specification on page 24 discloses the ability of truncated CRAF1 to inhibit CD40-mediated triggering of Ramos cells to upregulated CD23 but does not allegedly provide disclosure regarding CD40-mediated cell activation. The examiner stated that Hu et al. teach that CD40 activation is critical for B-cell proliferation, immunoglublin class switching, and rescue of germinal center B cells but does not address the metes and bounds of CD40 cell-mediated activation. Furthermore, the examiner stated that measurable, defined parameters that result after CD40 activation are not equivalent to and do not teach regarding the metes and bounds of "CD40-mediated cell activation." The examiner also stated that the specification contemplates that "activation" may include any and all intracellular signaling, immune responses, allergic responses, and apoptosis (pages 14-18), the metes and bounds of which are not clearly defined by a few specific examples. The examiner stated that "CD40 mediated cell activation" is vague and indefinite because it is not clear what measurable properties of "activation" correlate with CD40 mediated cell "activation," nor is it clear when a cell is determined to be "activated."

In reply, applicants respectfully traverse the rejection and maintain that the presently claimed invention is fully enabled by the specification. Applicants have introduced new claim 21 which recites SEQ ID NO: 1 which number corresponds to the amino acid sequence shown in Figure 1. Applicants maintain that new claim 21 obviates the other grounds of rejection. Therefore, applicants respectfully request that the examiner reconsider and withdraw this ground of rejection.

As to the term "CD40 mediated cell activation," applicants note that such term is no longer included in the pending claims. Therefore, this ground of rejection is moot.

Rejection Under 35 U.S.C. §112, first paragraph

The examiner maintained the rejection of claims 1, 3 and 4 under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention with regard to the determination of variants which inhibit CD40-mediated cell activation. The examiner withdrew all other bases of rejection.

The examiner stated that with regard to cell activation, applicant argues as above that one of skill would know how to determine CD40-mediated cell activation and its inhibition commensurate in scope with the claimed invention. The examiner stated that applicant refers again to Potocnik et al. and to the working example of CD23 upregulation. The examiner stated that "activation" may include (but is not limited to) any and all intracellular signaling, immune responses, allergic responses, and apoptosis (pages 14-18). It is the examiner's position that working examples of measurable, defined parameters that result after CD40 activation of specific cells are not equivalent to and do not teach regarding the full scope of "CD40-mediated cell activation." This is not rectified by the teachings of Potocnik et al. which do not address determination of CD40-mediated cell activation.

In reply, applicants respectfully traverse the rejection of claims 1, 3 and 4 under 35 U.S.C. §112, second paragraph. Applicants maintain that the presently claimed invention is particularly pointed out in the language of new claim 21. New claim 21 makes no reference to CD40 mediated cell activation and therefore, applicants maintain that this rejection is obviated. Applicants request the examiner to reconsider and withdraw this ground of rejection.

Rejection Under 35 U.S.C. §102(a)

The Examiner rejected claims 1, 3 and 4 under 35 U.S.C. §102(a) as being anticipated by Cheng et al. (Science 267:11494-1498, March 10, 1995 - IDS).

The examiner stated that Cheng et al. teach that truncated CRAF1, clone C26, identical to the instant product, inhibits CD40-mediated up-regulation of CD23. The examiner stated that applicants intention to file a declaration that Cheng et al. is not a publication by other is noted, however, until such time as this is established, Cheng et al. remains prior art.

In reply, applicants maintain that Cheng et al. is not a proper reference under 35 U.S.C. §102(a). Applicants submit herewith as **Exhibit 1** a Declaration Under 35 U.S.C. §1.132 of Dr. Seth Lederman, as evidence that David I. Hong (the only author of Cheng et al. who is not named as an inventor of the present application) did not contribute to the conception of the claimed invention. Accordingly, applicants request that the examiner reconsider and withdraw this ground of rejection.

Rejection Under 35 U.S.C. §102(b)

The examiner maintained the rejection of claims 1, 3, and 4 under 35 U.S.C. §102(b) as being anticipated by Sato et al. (FEBS Lett. 358:113-118, Jan. 23, 1995) or Hu et al. (J. Biol. Chem. 269:30069-30072, Dec.1994).

The examiner stated that applicant argues that Sato et al. does not teach the truncated protein as claimed because CAP1 is a different length that CRAF1 and there are numerous amino acid differences between CAP1 and CRAF1. The examiner stated that applicant concludes that since the proteins are different, so then are the truncated versions. The examiner took the position

that since the claims are not drawn to a full length protein, the length of the protein taught by Sato et al. is irrelevant so long as Sato et al. teach a peptide that meets the instant claim requirements. Also, the examiner stated that the instantly claimed truncated proteins encompasses conservative variants and thus the sequence of the art peptide need not be completely identical. Nevertheless, the examiner stated that sequence comparison between CRAF1 and Sato et a.l's CAP1 reveal two amino acid mismatches at positions 338 and 373 which are not included in the truncated protein taught by Sato et al. which begins at residue 384, after the mismatches. Thus, the examiner stated that the truncated protein of Sato et al., starting at CAP1 residue 384 and ending at CAP1 residue 540, including the TRAF domain and sufficient for binding CD40, is identical to the instantly claimed truncated proteins.

The examiner stated that applicant further argues that Hu et al. does not teach a truncated version of CD40bp but only teaches the full length protein and truncated TRAF2. The examiner pointed out that Hu et al. state on page 30072, column 2, lines 2-5:"...one class of interacting CD40bp cDNAs identified in the two-hybrid screen encoded only the C-terminal half of CD40bp (beginning at Phe 297, which deletes the RING finger and truncates the coiled-coil segment)."

In reply, applicants respectfully traverse the rejection and maintain that neither Sato et al. nor Hu et al. anticipate the presently claimed invention.

In order for a reference to anticipate the claimed invention, it must disclose every element of the claimed invention. Sato et al. do not disclose the protein as presently claimed. The presently claimed invention is directed to a class of polypeptides, approximately 80 in number, which range from 153 amino acids in length to 243 amino acids in length.

The examiner alleges that Sato et al. disclose a "truncated protein" starting at CAP-1 residue 384 and ending at CAP-1 residue 540. Applicants respectfully disagree. Sato et al. makes reference to the span of amino acids corresponding to positions 384-540 of their Figure 2 at the top of column 2 of page 117 and in the last sentence of the second paragraph of column 1 of page 117. Sato et al. state that "the TRAF domain of CAP-1 is located between residues 384 to 540...." Applicants maintain that the alleged truncated protein of 384-540 amino acids is **NOT** disclosed by Sato et al. On the contrary, Sato et al. merely disclose a structural characteristic of the larger CAP-1 sequence, that of containing a TRAF domain which falls between the internal residues at position 384 and position 540.

Separately, Sato et al. disclose a CAP-1 cDNA originally cloned during two hybrid yeast cDNA library screening encodes little more than the TRAF domain. Sato et al. do not disclose specfically which protein was encoded by the cDNA clone, and importantly, did not express and then isolate any protein encoded by it. Therefore, applicants' claimed isolated protein is not disclosed by Sato et al.

Hu et al. do not anticipate the presently claimed invention. Figure 4, panel E of Hu et al. discloses "homology within the c-terminal TRAF domains..." (see Figure 4, figure legend on page 30071 of Hu et al. Within Figure 4E of Hu et al., applicants point out two amino acid differences between the proteins of the claimed invention and that disclosed by Hu et al. First, at position number 390 of Hu et al., there is a methionine (M) and at the corresponding position of SEQ ID NO: 1 of the subject application, there is a threonine (T). Second, at position number 404 of Hu et al. there is a glycine (G) and at the corresponding position of SEQ ID NO: 1 of the subject application, there is an arginine (R). Neither of these substitutions are encompassed by the claimed invention.

Therefore, Hu et al. do not anticipate the claimed invention.

Thus, applicants maintain that the presently claimed invention is not anticipated by either Sato et al. or Hu et al.

In view of the above amendments and discussion, applicants respectfully request that the Examiner reconsider and withdraw the outstanding grounds for rejection and earnestly solicit the allowance of pending claims 3, 4 and 21.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone him at the number provided below.

No fee, other than the $435.00 extension of time fee, is deemed necessary in connection with the filing of this Amendment. However, if any additional fee is required, authorization is given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,

I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to:
Assistant Commissioner for Patents
Washington, D.C. 20231.

12/16/99

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